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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,844	09/10/1999	KATHERINE A. HIGH	10650/002002	3411

7590 02/24/2003

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EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/24/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/393,844	HIGH ET AL.
Examiner	**Art Unit**
Daniel M Sullivan	1636

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

This Non-Final Office Action is a response to the "Amendment and Response" filed 25 November 2002 (Paper No. 17) in reply to the Non-Final Office Action mailed 20 May 2002 (Paper No. 13). Claims 1-9 were considered in Paper No. 13. Claim 1 was amended and claims 10-17 were added in Paper No. 17.

Because the application as filed contained claims 10-20, which were canceled by amendment in Paper No. 4 (filed 10 September 1999), claims filed as 10-17 in Paper No. 17 have been entered as claims 21-28, respectively. Therefore, claims 1-9 and 21-28 are pending and under consideration in the application.

Claim Objections

Claims 22-24 are objected to because of the following informalities: As a consequence of the claims being renumbered, the dependency of the claims is incorrect. The claims should be amended such that they depend from the proper base claims. For the purpose of examination it has been assumed that claims 22 and 23 should depend from claim 21 and that claim 24 should depend from claim 23. Appropriate correction is required.

Response to Amendment

Claim Rejections - 35 USC § 102

Rejection of claims 1-3 and 6-8 under 35 U.S.C. § 102(e) as anticipated by Wiener *et al.* is withdrawn in view of the amendments to the claims and arguments of record in Paper No. 17.

Claim Rejections - 35 USC § 103

Rejection of claims 1-3 and 6-8 under 35 U.S.C. § 103(a) is withdrawn in view of the amendments to the claims and arguments of record in Paper No. 17.

Claim 9 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Weiner in view of Crabtree *et al.* for reasons of record in Paper No. 13. Applicant's arguments in Paper No. 17 regarding the patentability of the claim are based on the limitation of claim 1 to a virus. However, claim 9 is directed to a kit including the vector of claim 1, which is comprised within the virus of claim 1. Therefore, claim 9 is not limited to a virus and remains unpatentable over the prior art for the reasons of record.

Newly added claims 21-28 are free of the art of record for reasons provided under the heading of "Allowable Subject Matter" in Paper No. 6.

New Grounds for Rejection

Double Patenting

Applicant is advised that should claims 6-9 be found allowable, claims 25-28 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In the interest of compact prosecution, the claims have been examined on the merits with the assumption that applicant intends that the claims depend from claim 21, rather than claim 1. Amending the claims accordingly would be remedial.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 21-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims of the instant application are directed to a composition comprising a virus, which virus comprises a DNA encoding a Factor IX gene or a Factor IX gene comprising a mutation which renders the Factor IX encoded thereby incapable of binding collagen IV. The specification teaches that Factor IX encompasses all mammalian Factor IX sequences (page 15,

paragraph 3), all naturally occurring variants or recombinantly derived mutants of wild-type Factor IX which mutations render it therapeutically effective or more therapeutically effective (paragraph bridging pages 15 and 16), variants which retain Factor IX biological activity, variants that confer enhanced stability on the protein variants having enhanced specificity of action (page 16, paragraph 3). In the first full paragraph on page 17, the specification states that the amino acid sequence of a human Factor IX analog has about 70% or greater homology with the amino acid sequence described in Yoshitake *et al.* The claims therefore broadly encompass a composition comprising a DNA encoding any polypeptide having the same or improved biological activity relative to the biological activity of wild-type human Factor IX. Biological activity is defined in the paragraph bridging pages 18 and 19 of the specification as, "capable of mediating coagulation of blood in a blood coagulation assay." As the limitations on structure are set forth only as preferred embodiments, the polypeptide need not be structurally similar to a polypeptide having Factor IX biological activity at all. However, because the disclosure fails to provide adequate written description for even the more limited embodiments wherein the polypeptide has 70%, 80% or 90% homology with the sequence of Yoshitake *et al.*, the structural limitations will be read into the claims for the purpose of explaining the basis for this rejection. Obviously, those embodiments having no structural limitation also fail to meet the written description requirements for the reasons set forth below.

The Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Federal Register, Vol. 66, No. 4, Column 3, page 71434). As the instant claims are limited to a

composition comprising a Factor IX gene, the Factor IX gene is a critical element of the claimed composition and must be adequately described. The teachings from the specification cited herein above demonstrate that the Factor IX encoded by the gene of the claims is a genus of polypeptides having Factor IX biological activity. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). The instant disclosure cites several publications of genes encoding human Factor IX and Factor IX from mouse, canine, rabbit and bovine (see especially page 15, paragraph 3). The specification also teaches a variant of human Factor IX having reduced binding to collagen IV as a consequence of substitution of an alanine residue in place of a lysine at position five in the mature Factor IX polypeptide. Thus, the specification discloses 5 species of mammalian Factor IX and a single example of a Factor IX having reduced binding to collage IV. However, given the enormous scope and divergent nature of the subject matter encompassed by the Factor IX of the claims, these examples fail to adequately represent the full genus. It is therefore incumbent upon Applicant to disclose the characteristics that identify the genus of molecules encompassed by Factor IX.

According to the Guidelines for written description, identifying characteristics include, "structure or other physical and/or chemical properties...functional characteristics coupled with a known or disclosed correlation between function and structure or... a combination of such identifying characteristics..." (Federal Register, Vol. 66, No. 4, page 1106, column 3, second full paragraph). To the extent that Factor IX might be limited to a polypeptide that is structurally related to a disclosed polypeptide sequence, in order to fully describe the structure of a

polypeptide Applicant must describe more than simply the primary amino acid sequence because the functionality of a polypeptide is comprised within its higher order structure (i.e. secondary and tertiary structure). Because it is presently impossible to envision the higher order structure of a polypeptide based on a description of its primary structure alone, the skilled artisan would not recognize that Applicant was in possession of the broad genus of polypeptides having Factor IX biological activity based on a description of the primary structure of any and all variants of Factor IX. As indicated in the Revised Interim Guidelines cited herein above, a genus of polypeptides might also be adequately described by disclosure of structural characteristics coupled with correlation of those structural characteristics with functional properties of the polypeptide. The instant disclosure is silent regarding the structural determinants of Factor IX biological activity and particularly fails with regard to the structural features underlying the enhanced biological activity encompassed by the Factor IX of the claims. Outside of the alanine substitution for lysine at position 5, the disclosure teaches no correlation of structure to enhanced biological activity at all.

The specification also teaches how Factor IX mutants might be generated and tested for biological activity (see especially the paragraph bridging pages 17 and 18). However, An adequate written description of a polypeptide, or DNA encoding a polypeptide, requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polypeptide itself. It is not sufficient to define polypeptide solely by its principal biological property, i.e. it has Factor IX biological activity, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically

known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all polypeptides that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of DNA's encoding polypeptides having Factor IX biological activity. Therefore, only the described DNA encoding wild-type human, mouse, canine, rabbit and bovine Factor IX and human Factor IX comprising a mutation encoding an alanine residue in place of a lysine in the fifth amino acid position from the beginning meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 28 are indefinite in being directed to a kit including the vector of claim 1. As pointed out herein above, the claims read as though the kit comprises only the vector

component of the composition and not the entire virus. It would seem logical, however, that the kit should comprise the entire composition of the claim.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
February 14, 2003

KETTER
PRIMARY EXAMINER

JAMES KETTER
PRIMARY EXAMINER